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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,456	11/13/2003	Lawrence G. Hamann	LA0091 NP	9300

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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/712,456	Applicant(s) HAMANN ET AL.	
	Examiner Venkataraman Balasubramanian	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' response, which included amendment to claims 1, 2, 8 and 9, filed on 4/5/2006, is made of record. Claims 1-9 are pending.

In view of applicants' response, 112 second paragraph rejections and 112 first paragraph rejection as applied to prodrug, have been obviated. However, the following apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 9 are rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating breast cancer and prostate cancer, does not reasonably provide enablement for treating all diseases embraced in the claim 8. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims.

Method claims 8 and 9 are not adequately enabled for treating several diseases generically embraced in the instant claim 8. From the reading of specification, it appears that the applicants are asserting that the embraced compounds because of their mode action as of modulator of androgen receptor, would be useful for treating any or all diseases, for which, there is no supporting disclosure in the specification.

As recited these method of use claims are Reach through Claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic

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functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification.

In the instant case, it appears that, because the instant compounds modulate androgen receptor, it is recited that, based on this modulation of AR, all diseases of claim 8 can be treated with the instant compounds for which there is no adequate written description and enabling disclosure. Besides the long list of diseases recited in specification in pages 19-21, claim 8 also recites a list of several diseases for which also there is no enabling disclosure. More specifically, claim 8 recites a method for treating or delaying the progression or onset of muscular atrophy, sarcopenia, frailty or age-related functional decline, reduced muscle strength and function, reduced bone density or growth, chronic fatigue syndrome, bone fracture repair, acute fatigue syndrome and muscle loss following elective surgery, cachexia, eating disorders, side effects of chemotherapy, wasting, depression, growth retardation, male contraception, hypogonadism, for which there is no adequate written description and enabling disclosure.

Specification on pages 30-41 teaches an assay modulation of AR and it is asserted therefore that the instant compounds would be useful for treating any or all diseases stated above. However, there is no competent evidence in the specification that such an inhibition in the assay conditions would result in the effective treatment of any or all of these diseases. Moreover many if not most, several of these diseases are very difficult to treat and at present there is no known drug, which can successfully be used to treat all diseases related androgen. Despite the fact there are several

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androgen modulators are available, it is still difficult to treat several diseases dependent on steroids.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288 . Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See *Fernand Labrie*, *International Braz. J. Urol.* 30(1): 3-11, 2004 and *Taplin et al.*, *J. Cell Biochem.* 91(3): 493-90 (PubMed Abstract provided).

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating all diseases embraced in claim 8 that require AR modulation of instant compound.

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2) The state of the prior art: Although there are large number steroid modulating agents known (see instant IDS- NPL references), none of them are claimed or shown to be useful in treating all such diseases.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds for treating any or all diseases stated above. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples for treating all such disease that require AR modulation and the state of the art is that the effects of such agents based on the disclosed inhibitory activity are unpredictable. See Labrie and Taplin et al. cited above.

6) The breadth of the claims: The instant claims embrace several diseases including those yet to be related to instant AR activity.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant

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case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of receptor-ligand interactions in general, and the lack of working examples regarding the activity of the claimed compounds toward treating variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

This rejection is same as made in the previous office action but now limited selected diseases. Applicants' traversal to overcome this rejection is not persuasive. Applicants may provide literature related treating all the diseases or some of them with objective enablement for the remaining.

Prior art search did not as noted before lend support for treating all the diseases embraced in claim 8.

Hence, this rejection is proper and is maintained.

Claim Rejections - 35 USC § 102

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 5-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Morihira et al., WO 02/18335 for reasons of record. To repeat:

Morihira et al. teaches several pyrrolidine compounds for treating CCR3-mediated diseases, which include instant compounds. See entire document especially pages 1-16 for details of the invention. Especially see Table 2-18 for various compounds, which include instant compounds with generic G definition.

Applicants' argument to overcome this rejection is not persuasive. Applicants are urged to look at compounds shown in Table 2-18, pages 57-78. These compounds are also claimed in the instant claims. See G definition. This rejection is proper and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 5-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morihira et al., WO 02/1833 for reasons of record. To repeat:

Teachings of Morihira et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Morihira et al. teaches several pyrrolidine compounds for treating CCR3-mediated diseases which include instant compounds. See entire document especially pages 1-16 for details of the invention.. Especially see Table 2-4 for various compounds which include instant compounds with generic G definition.

Morihira et al. differs from the instant claims in exemplifying only limited number of compounds of the genus of compounds claimed as seen in pages 1-16

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However, Morihira et al. teaches equivalency of those compounds taught in Table 2-4 with those generically recited in pages 1-16.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Morihira et al and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants' argument to overcome this rejection is not persuasive. Applicants are urged to look at compounds shown in Table 2-18, pages 57-78. These compounds are also claimed in the instant claims. See G definition. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Morihira et al and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

This rejection is proper and is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is (571) 272-0661.

The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

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6/26/2006